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PHOTO QUIZ

Answer to Photo Quiz: Pulmonary and Cardiovascular Manifestations of SARS-CoV-2 Infection

Isaac H. Solomon,[a,b] Robert F. Padera, Jr.[a,b]

[a]Department of Pathology, Brigham and Women's Hospital, Boston, Massachusetts, USA
[b]Department of Pathology, Harvard School of Medicine, Boston, Massachusetts, USA

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was found to be present by reverse transcriptase PCR (RT-PCR) targeting N1 and N2 gene products, performed by the Massachusetts Department of Public Health on a postmortem nasopharyngeal swab (1), confirming the diagnosis of coronavirus disease 2019 (COVID-19). In addition, immunohistochemistry performed at Brigham and Women's Hospital, using a rabbit polyclonal antibody targeting the severe acute respiratory syndrome coronavirus (SARS-CoV) nucleocapsid (NB100-56576; Novus Biologicals, Centennial, CO) (2), was strongly positive in pneumocytes as well as occasional histiocytes, supporting COVID-19 as the etiology of the diffuse alveolar damage.

SARS-CoV-2 is a betacoronavirus, thought to have originated from bats, that was first recognized in Wuhan, China, in December 2019 and has since been declared a worldwide pandemic, with >5 million confirmed cases and >300,000 deaths as of May 2020 (https://coronavirus.jhu.edu/map.html; accessed 23 May 2020). Virus is spread primarily through the inhalation of respiratory droplets or aerosolized particles and can be spread by asymptomatic/presymptomatic individuals, allowing for efficient dissemination among a nonimmune population. Older adults, people living in nursing homes, and individuals with severe comorbidities, including pulmonary disease, cardiovascular disease, diabetes mellitus, and severe obesity, are at the highest risk for severe COVID-19, often requiring mechanical ventilation and resulting in death. Laboratory confirmation typically occurs by RT-PCR on nasopharyngeal swabs, while serology is more useful later in the disease course and for epidemiological purposes (3).

The mechanisms underlying SARS-CoV-2 pathogenesis are incompletely understood. Virus utilizes host angiotensin-converting enzyme 2 (ACE2) for cellular uptake and transmembrane protease serine 2 (TMPRSS2) for priming of the viral spike protein, and viral tropism is thought to be dependent on the expression levels of these two genes (4). Insights have been gained from initial autopsy case series, which show the highest concentration of virus and disease burden in the lungs, consisting of diffuse alveolar damage, microthrombosis, occasional bronchopneumonia, and pulmonary embolism (2, 5). Additional sites of damage include heart, liver, brain, and kidneys, which generally lack significant inflammation or necrosis, and this damage is likely due to a combination of cytokine storm, microthrombosis, hypoxemia, and ischemia rather than a direct effect of viral infection. There are no characteristic viral cytopathic effects associated with SARS-CoV-2 infection, and it is important not to mistake prominent reactive nuclei or internalized cellular debris for viral inclusions, especially within the lung. Due to the overlap of histological features with other infectious (including SARS-CoV and Middle East respiratory syndrome coronavirus) and noninfectious causes of diffuse alveolar damage, this diagnosis requires sufficient clinical suspicion with confirmation by ancillary techniques such as immunohistochemistry or RT-PCR. SARS-CoV-2 infection can cooccur with other respiratory bacterial and viral infections, further

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Address correspondence to Robert F. Padera, Jr., rpadera@bwh.harvard.edu.

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complicating the histological differential. Thrombi are generally not subtle and can be recognized microscopically by pale eosinophilic material occluding a blood vessel lumen. Coagulopathy in COVID-19 is associated with increased risk of death, with laboratory testing revealing increased levels of D-dimer, lactate dehydrogenase, and ferritin (6). Whether increased rates of pulmonary embolism are due to specific effects of the virus has yet to be resolved (7).

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